

#14A  
1/18/04  
8/13/02

AMENDMENT

Please amend the application as follows:

In the specification:

Please replace the paragraph beginning at page 1, line 1 with the following rewritten paragraph:

A1 -- This application is a Continuation-in-Part application of co-pending U.S. Patent Application Serial No. 09/391,340, filed September 7, 1999, which is a divisional of U.S. Patent Application Serial No. 08/907,166, filed August 6, 1997, now issued as U. S. Patent No. 5,948,666. --

Please replace the paragraph beginning at page 3, line 23 with the following rewritten paragraph:

A2 -- Another aspect of the invention is an isolated nucleic acid encoding a polypeptide or a functional fragment thereof having a sequence as set forth in SEQ ID NO:2 and sequences substantially identical thereto. --

Please replace the paragraph beginning at page 5, line 21 with the following rewritten paragraph:

A3 -- Another aspect of the invention is an assay for identifying fragments or variants of SEQ ID NO: 2, and sequences substantially identical thereto, which retain the extreme high temperature polymerase activity of the polypeptides of SEQ ID NO: 2 (i.e., at temperatures of 95°C to 113° C, for four or more hours. The assay includes utilizing a polypeptide encoded by a nucleic acid having at least 70% homology to SEQ ID NO: 1, and sequences substantially identical thereto, or polypeptide fragment or variant encoded by SEQ ID NO: 1, to effect DNA polymerase activity in a PCR amplification at extreme high temperature for four or more hours and under conditions that allow said polypeptide or fragment or variant to function, and detecting formation of an amplification product, wherein formation of the amplification product is indicative of a functional DNA polymerase polypeptide or fragment or variant. --

Please replace the paragraph beginning at page 18, line 14 with the following rewritten paragraph:

A4 -- In one embodiment, the ligation reassembly process is performed exhaustively in order to generate an exhaustive library. In other words, all possible ordered combinations of the nucleic acid building blocks are represented in the set of finalized chimeric nucleic acid molecules. At the same time, the assembly order (i.e. the order of assembly of each building block in the 5' to 3' sequence of each finalized chimeric nucleic acid) in each combination is by design (or non-stochastic). Because of the non-stochastic nature of the method, the possibility of unwanted side products is greatly reduced. --

Please replace the paragraph beginning at page 26, line 30 with the following rewritten paragraph:

AS -- Therefore, in one embodiment, the invention relates to a method for producing a biologically active hybrid polypeptide and screening such a polypeptide for enhanced activity by:

- 1) introducing at least a first polynucleotide in operable linkage and a second polynucleotide in operable linkage, said at least first polynucleotide and second polynucleotide sharing at least one region of partial sequence homology, into a suitable host cell;
- 2) growing the host cell under conditions which promote sequence reorganization resulting in a hybrid polynucleotide in operable linkage;
- 3) expressing a hybrid polypeptide encoded by the hybrid polynucleotide;
- 4) screening the hybrid polypeptide under conditions which promote identification of enhanced biological activity; and
- 5) isolating the polynucleotide encoding the hybrid polypeptide. --